IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Nobuo Mochizuki, et al.
Application No.: 10/553, 108
Filed: October 12, 2005
Confirmation No.: 8647
Art Unit: 1626
Examiner; Havlin, Robert H.
For: PHENYLAZOLE COMPOUND, PRODUCTION PROCESS THEREFOR AND ANTIOXIDANT

DECLARATION UNDER 37 CFR § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Seiichi Uchida, hereby declare and state that:

1. I am a citizen of Japan, residing at 524-17, Higashi-koiso Oiso-machi, Naka-gun, Kanagawa, 255-0004, Japan.

2. I am one of the inventors of the subject application, and I am fully familiar with the subject matter thereof as well as the references relied upon by the Examiner in the prosecution of this application.

3. I obtained a Master's degree from in department of pharmaceutical sciences from Nagoya City University in March, 1982, where I studied the zymology of the lysosomal ATPase of chicken's liver.

4. I am currently employed by Nippon Soda Co., Ltd., and began working for Nippon Soda Co., Ltd., in April, 1982, whereat I have been engaged in research on drug discovery.

5. In order to demonstrate unexpected effects of difference between the present invention and the cited reference, namely US Patent No. 6,342,516 by Umeda, et al., I

conducted the following comparative test using Compounds 1 and 2 disclosed in the present specification and Compounds 3-1 and 3-9 disclosed in the cited reference (hereinafter, abbreviated as "516" patent) as each test compounds.

(Method)

Each tissue migration of the test compounds was evaluated by measuring the antioxidative action on lipids *ex vivo*. Each test compound was dissolved in dimethyl sulfoxide (DMSO, with a final concentration of 20% by mass), and then suspended in an aqueous physiological saline solution containing 1% by mass of polyethylene hardened castor oil (manufactured by Nikko Chemicals Co., Ltd., under the trademark of NIKKOL HCO-60). Each obtained sample was administered orally to three male SD rats (aged 6 weeks, purchased from Japan SLC, Inc.) at a dose of 100 mg/kg. In a control-administration group, a mixture liquid in which 20% by mass of DMSO and 1% by mass of polyethylene hardened castor oil were formulated in an aqueous physiological saline solution was administered orally to three male SD rats at the same dose as that of each group described above . An hour after the administration, each brain of the animals was removed under anesthesia. The lipid peroxide activity in a homogenate of each brain was measured in the same way as that of Example 3 described in the present specification. The inhibition rate of each test compound in the brain was determined from the amounts of lipid peroxide formed in the control-administration group and each test compound-administration group. The results are shown in the following table.

(Results)

Compound No.	Inhibition rate of *ex vivo* lipid peroxide action in the brain (%)
Compound 2	97 ± 0.9
Compound 3-1 ("516" patent)	45 ± 21.0
Compound 1	83 ± 12.1
Compound 3-9 ("516" patent)	22 ± 31.5

As is apparent from the results, Compounds 1, and 2 according to the present invention exhibited significant medicinal benefits even on the brain, in comparison with Compounds 3-1 and 3-9 disclosed in "516" patent.

(Conclusion)

The above-mentioned results suggest that unexpected effects are exhibited by Compounds 1 and 2.

6. I fully understand the content of this declaration.

7. I, Seiichi Uchida, the undersigned declarant, declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine, imprisonment, or both, under section 1001, of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed this 21 day of April, 2009.

Seiichi Uchida

(Seiichi Uchida)